

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

10 Jun 2026

### Effect of Methotrexate on Symptoms and Nasal Polyp Size in Patients With Recurrent Chronic Rhinosinusitis With Nasal Polyps (CRSwNP): A Double-Blind Randomized Pilot Clinical Trial

#### Protocol summary

(Lund-Kennedy); Secondary outcomes: SNOT-22 score, Symptom severity score

#### Study aim

Effect of Methotrexate on Symptoms and Polyp Size in Patients With recurrent Chronic rhino sinusitis with nasal polyposis (CRSwNP)

#### Design

This study is a Phase III randomized, double-blind, placebo-controlled Pilot clinical trial conducted on 40 patients. Randomization and allocation of participants into two groups were performed using the website <https://sealedenvelope.com/randomisation>.

#### Settings and conduct

This is a randomized, double-blind, parallel pilot clinical trial (1:1) conducted in adult patients with recurrent CRSwNP at Imam Khomeini Hospital, Ahvaz. Participants are randomly assigned to oral methotrexate or placebo group, with 12-week follow-up. Both patients and outcome assessors are blinded, and the placebo is matched in appearance and dosing schedule.

#### Participants/Inclusion and exclusion criteria

Inclusion criteria: Age  $\geq 18$  years; diagnosis of recurrent CRSwNP based on EPOS 2020 criteria (European position paper on Rhinosinusitis and Nasal polyps); no use of biologics in the past 6 months; written informed consent. Exclusion criteria: Active liver disease; severe hematologic abnormalities (WBC  $< 3,000/\mu\text{L}$  or PLT  $< 100,000/\mu\text{L}$ ); renal impairment (CrCl  $< 50$  mL/min); active infection (TB, HBV, HCV); known hypersensitivity to methotrexate.

#### Intervention groups

Intervention: oral methotrexate (Nanovalond) 15 milligrams weekly for 12 weeks. Control: oral methotrexate placebo 15 milligrams weekly for 12 weeks. All patients: weekly folic acid five milligrams (Shefa), intranasal fluticasone spray (Koushan Pharmed), and nasal rinse (Sgalesh).

#### Main outcome variables

Primary outcome: Nasal endoscopy score

#### General information

##### Reason for update

##### Acronym

##### IRCT registration information

IRCT registration number: **IRCT20120404009375N2**

Registration date: **2026-05-10, 1405/02/20**

Registration timing: **registered\_while\_recruiting**

Last update: **2026-05-10, 1405/02/20**

Update count: **0**

##### Registration date

2026-05-10, 1405/02/20

##### Registrant information

##### Name

Soheila Nikakhlagh

##### Name of organization / entity

Ahvaz Jondishapoor University of Medical Sciences

##### Country

Iran (Islamic Republic of)

##### Phone

+98 61 3292 1838

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nikakhlagh-s@ajums.ac.ir

##### Recruitment status

**recruiting**

##### Funding source

##### Expected recruitment start date

2026-03-10, 1404/12/19

##### Expected recruitment end date

2026-09-21, 1405/06/30

##### Actual recruitment start date

empty

**Actual recruitment end date**

empty

**Trial completion date**

empty

**Scientific title**

Effect of Methotrexate on Symptoms and Nasal Polyp Size in Patients With Recurrent Chronic Rhinosinusitis With Nasal Polyps (CRSwNP): A Double-Blind Randomized Pilot Clinical Trial

**Public title**

Effect of Oral Methotrexate on Improvement of Nasal Polyps

**Purpose**

Treatment

**Inclusion/Exclusion criteria****Inclusion criteria:**

Age 18 or greater than Diagnosis of recurrent Chronic Rhinosinusitis With Nasal Polyps (CRSwNP) based on the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS 2020) criteria No use of biological medications during the past six months Written informed consent for participation in the study

**Exclusion criteria:**

Presence of active liver disease Severe leukopenia or thrombocytopenia, defined as White Blood Cell count (WBC) less than 3,000 per microliter or Platelet count (PLT) less than 100,000 per microliter Significant renal dysfunction defined as Creatinine Clearance (CrCl) less than 50 milliliters per minute Active infection with Mycobacterium tuberculosis (TB), Hepatitis B virus (HBV), or Hepatitis C virus (HCV) Alcohol abuse Known hypersensitivity to methotrexate

**Age**

From **18 years** old to **60 years** old

**Gender**

Both

**Phase**

3

**Groups that have been masked**

- Participant
- Outcome assessor

**Sample size**

Target sample size: **40**

**Randomization (investigator's opinion)**

Randomized

**Randomization description**

Participants will be randomly allocated into two study groups using the SealedEnvelope.com/randomisation website. Block randomization with variable block sizes (4 or 6) with a 1:1 allocation ratio will be used. The randomization process will be performed by an epidemiologist

**Blinding (investigator's opinion)**

Double blinded

**Blinding description**

This study will be conducted in a double-blind manner (participants and outcome assessor/examining physician). The study drug and placebo will have identical packaging and labeling. Participant assignment

will be concealed using alphanumeric codes (concealment). The randomized code list will be kept in two copies by the study epidemiologist and the principal investigator, and will only be broken in case of emergency.

**Placebo**

Used

**Assignment**

Parallel

**Other design features****Secondary Ids**

empty

**Ethics committees****1****Ethics committee****Name of ethics committee**

Ethical Committee of Ahvaz Jundishapur University of Medical Sciences

**Street address**

College Town, Golestan

**City**

Ahvaz

**Province**

Khuzestan

**Postal code**

6135715794

**Approval date**

2026-02-21, 1404/12/02

**Ethics committee reference number**

IR.AJUMS.REC.1404.656

**Health conditions studied****1****Description of health condition studied**

Patients With Recurrent Chronic Rhinosinusitis With Nasal Polyps

**ICD-10 code**

J33.0

**ICD-10 code description**

Polyp of nasal cavity

**Primary outcomes****1****Description**

Nasal endoscopy score base on Lund-Kennedy score

**Timepoint**

At baseline (prior to the start of the intervention, week 0), and subsequently at weeks 4, 8, and 12 after the initiation of the intervention

**Method of measurement**

Endoscopic evaluation of the nasal cavity scored using the Lund-Kennedy index

## Secondary outcomes

### 1

#### Description

Sino Nasal Outcome 22 questionnaire score

#### Timepoint

At baseline (prior to the start of the intervention, week 0), and subsequently at weeks 4, 8, and 12 after the initiation of the intervention

#### Method of measurement

Sino-Nasal Outcome Test-22 Questionnaire

### 2

#### Description

score of severity of symptoms (nasal congestion, nasal discharge, decreased sense of smell, and facial pain or pressure)

#### Timepoint

At baseline (prior to the start of the intervention, week 0), and subsequently at weeks 4, 8, and 12 after the initiation of the intervention

#### Method of measurement

Patient-reported symptom severity will be measured using the Visual Analog Scale

## Intervention groups

### 1

#### Description

Intervention group: Patients will receive oral methotrexate at a dose of 15 mg per week for 12 weeks, administered as divided doses over two consecutive days (Thursday and Friday). The methotrexate used is Trexoma® 2.5 mg tablets (Nano Alvand Pharmaceutical Nanotechnology Company). In addition, folic acid 5 mg will be administered once weekly (Shafa Pharmaceutical and Hygienic Company). All patients will receive standard therapy, including intranasal fluticasone spray twice daily (Koushan Pharmed Company) and nasal and sinus irrigation with saline solution 1-2 times daily (SGALESH Nasal and Sinus Irrigation Solution). In case of severe exacerbation of symptoms, a short course (up to one week) of oral prednisolone (Aburaihan Pharmaceutical Company) may be prescribed. The dose and duration of prednisolone use will be recorded and considered in the data analysis.

#### Category

Treatment - Drugs

### 2

#### Description

Control group: patients will receive placebo tablets matching oral methotrexate at a dose equivalent to 15 mg per week, administered as divided doses on two consecutive days (Thursday and Friday) for a duration of 12 weeks. The placebo tablets will be prepared to resemble Trexoma 2.5 mg tablets manufactured by Nano Alvand Pharmaceutical Nanotechnology Company.

Additionally, folic acid 5 mg will be prescribed once weekly. The folic acid used in this study is manufactured by Shafa Pharmaceutical and Hygienic Company. All patients will also receive standard therapy, including intranasal fluticasone spray twice daily manufactured by Koushan Pharmed Company, and nasal and sinus irrigation with saline solution one to two times daily using SGALESH Nasal and Sinus Irrigation Solution. In case of severe exacerbation of symptoms, oral prednisolone manufactured by Aburaihan Pharmaceutical Company may be prescribed for a short course of up to one week. The dose and duration of prednisolone use will be carefully recorded and considered in the data analysis.

#### Category

Treatment - Drugs

## Recruitment centers

### 1

#### Recruitment center

##### Name of recruitment center

Imam Khomeini Hospital, Ahvaz

##### Full name of responsible person

Soheila Nikakhlagh

##### Street address

Otorhinolaryngology Department, Imam Khomeini Hospital, 24-Metri Street, Ahvaz, Khuzestan Province, Iran

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## Sponsors / Funding sources

### 1

#### Sponsor

##### Name of organization / entity

Ahvaz University of Medical Sciences

##### Full name of responsible person

Abdollah Rafiei

##### Street address

Vice-Chancellor for Research and Technology, Ahvaz Jundishapur University of Medical Sciences, Golestan Boulevard, Ahvaz, Iran

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**Grant name**  
Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

**Grant code / Reference number**  
HRC-0405

**Is the source of funding the same sponsor organization/entity?**  
Yes

**Title of funding source**  
Ahvaz University of Medical Sciences

**Proportion provided by this source**  
100

**Public or private sector**  
Public

**Domestic or foreign origin**  
Domestic

**Category of foreign source of funding**  
*empty*

**Country of origin**

**Type of organization providing the funding**  
Academic

## Person responsible for general inquiries

### Contact

**Name of organization / entity**  
Ahvaz University of Medical Sciences

**Full name of responsible person**  
Soheila Nikakhlagh

**Position**  
Professor

**Latest degree**  
Specialist

**Other areas of specialty/work**  
Ear, Nose, and Throat

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## Person responsible for scientific inquiries

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## Person responsible for updating data

### Contact

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**Other areas of specialty/work**  
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## Sharing plan

### Deidentified Individual Participant Data Set (IPD)

Undecided - It is not yet known if there will be a plan to make this available

### Study Protocol

Yes - There is a plan to make this available

**Statistical Analysis Plan**

Yes - There is a plan to make this available

**Informed Consent Form**

Yes - There is a plan to make this available

**Clinical Study Report**

Yes - There is a plan to make this available

**Analytic Code**

Undecided - It is not yet known if there will be a plan to make this available

**Data Dictionary**

Undecided - It is not yet known if there will be a plan to make this available

**Title and more details about the data/document**

**When the data will become available and for how long**

**To whom data/document is available**

**Under which criteria data/document could be used**

**From where data/document is obtainable**

**What processes are involved for a request to access data/document**

**Comments**